PM0344

THAT WHICH IS CLAIMED IS:

1. A ventilator system having a ventilation flow path for ventilating a subject, comprising:

a mass flow controller;

a gas delivery valve disposed downstream of and in communication with the mass flow controller, the gas delivery valve being configured to selectively dispense a plurality of different gases to a subject;

a first gas source in fluid communication with the gas delivery valve;

a second gas source in fluid communication with the gas delivery valve;

a first pressure sensor located upstream of the gas delivery valve;

a second pressure sensor located downstream of the gas delivery valve; and

a controller operatively associated with the first and second pressure sensors and the mass flow controller, the controller configured to monitor the pressures measured by the first and second pressure sensors and the flow rate of the mass flow controller and automatically determine a delivered tidal volume using a reading of the flow rate of the mass flow controller when the first pressure is at a substantially steady state condition.

2. A ventilator system according to Claim 1, wherein the controller is configured to automatedly adjust the flow rate of the mass flow controller so that the pressure measured by the first pressure sensor is substantially constant during delivery of hyperpolarized gas.

3. A ventilator system according to Claim 2, wherein the first gas source is a polarized gas source and the second gas source is a non-polarized gas source, said system further comprising a tracheal tube in fluid communication with the gas delivery valve, wherein the gas delivery valve is configured with a vent port that allows expired breath to vent during expiration, and wherein the gas delivery valve is configured to operate at a selectable breath per minute rate and inhale/exhale ratio

with a breath-hold duration and to selectively deliver the polarized gas alone or with the non-polarized gas.

4. A ventilator system according to Claim 1, wherein the system is configured to be run in a user selectable set tidal volume mode or a set peak inspiration pressure mode.

5. A ventilator system according to Claim 1, wherein the mass flow controller has a variable mass flow rate, and wherein the controller is configured to dynamically monitor the first pressure and adjust the flow rate of the mass flow controller responsive thereto to deliver a user-selected predetermined fixed tidal volume.

6. A ventilator system according to Claim 3, wherein the controller is configured to calculate an adjusted delivered tidal volume *in situ* based on the difference between a the total tidal volume and a fixed geometric volume of the ventilator flow path that includes a portion of the ventilator flow path and the tracheal tube.

7. A ventilator system according to Claim 1, wherein the controller is configured to determine the delivered tidal volume using the mathematical relationship:

flow rate/frequency= volume exhausted per cycle (1),

where the flow rate is the flow rate of the mass flow controller taken when the first pressure is substantially stable or constant and frequency is the breath per minute rate.

8. A ventilator according to Claim 7, further comprising a temperature monitor in communication with the controller.

9. A ventilator according to Claim 8, wherein the temperature monitor is in communication with a thermal source that is configured to heat and/or cool a subject to a desired temperature during operation.

10. A ventilator system according to Claim 3, further comprising a tracheal tube end cap for closing off the tracheal tube, wherein said gas delivery valve comprises a plurality of gas actuation valves in communication with a plurality of gas flow paths for selecting at least one gas flow path therein, said system further comprising computer program code for calculating a fixed volume "V1".

11. A ventilator system according to Claim 3, wherein the ventilator system is configured for small animals.

12. A ventilator system according to Claim 11, wherein the controller is configured to generate an estimated incremental decrease or increase of flow rate to provide a substantially constant pressure at the first sensor based on a selected breath per minute rate and an estimated volume of the animal's lungs.

13. A ventilator system according to Claim 11, wherein the controller is operably associated with computer program code of a library of *a priori* values of predicted animal volumetric characteristics and/or animal volumetric changes at a plurality of different peak inspiration pressures.

14. A ventilator system according to Claim 11, wherein the ventilator system is configured to deliver a millimole amount of polarized $^{129}Xe$ gas and/or polarized $^{3}He$.

15. A ventilator system according to Claim 11, wherein the ventilator is configured to operate with selectable breath per minute rates in the range of about 5-180.

16. A ventilator system according to Claim 1, wherein the polarized gas source comprises a pressure vessel holding a bag of polarized gas therein, wherein the bag of polarized gas is compressible by the controlled pressure of a non-polarized gas directed into the vessel, and wherein the system further comprises computer program code that calculates and applies a calibration factor to define the pressure used to compress the bag to expel a desired amount of polarized gas.

17. A ventilator system according to Claim 16, wherein the ventilator is configured to operate with selectable inspiration/expiration ratios from between about 5:1 to 1:5.

18. A ventilator system according to Claim 11, wherein the ventilator system is configured to operate with a controllable peak inspiration pressure of between about 0-40 inches of $H_20$.

19. A ventilator system according to Claim 18, wherein the ventilator is configured to provide a tidal volume flow of between about 0-5 liters/min.

20. A ventilator system according to Claim 11, wherein the ventilator system is configured to operate with MRI/NMR systems having up to about 5T magnetic fields.

21. A ventilator system according to Claim 11, wherein the ventilator system is configured to operate with MRI/NMR systems having less than about 100 Gauss magnetic fields.

22. A ventilator system according to Claim 1, further comprising a physiological monitor for monitoring heart rate and an ECG (electrocardiogram) device.

23. A ventilator system according to Claim 3, wherein the gas delivery valve is configured to provide gas flow paths for ventilation breath inhale inputs and/or receive exhale outputs of at least: (a) hyperpolarized Gas A inhale; (b) exhale; (c) hyperpolarized Gas A inhale and hold; and (d) non-polarized gas input.

24. A ventilator system according to Claim 23, wherein the gas delivery valve is configured to provide ventilation breath inhale inputs and/or receive exhale outputs of at least: (a) hyperpolarized Gas A inhale; (b) non-polarized Gas B inhale; (c) a combination of hyperpolarized Gas A and non-polarized Gas B inhale; (d) exhale; (e) partial exhale and hold; (f) hyperpolarized Gas A inhale and hold; (g) Gas B inhale and hold; and (h) a combination of hyperpolarized Gas A and Gas B inhale and hold.

25. A ventilator system according to Claim 24, wherein the gas delivery valve is fabricated from and/or coated with a material that inhibits depolarization of the hyperpolarized gas and is non-magnetic.

26. A ventilator system according to Claim 1, wherein the system has an associated fluid capacitance disposed intermediate the mass flow controller and the gas delivery valve.

27. A method of delivering hyperpolarized gas to a subject, comprising:

providing a ventilator system with a mass flow controller, a tracheal tube and a gas delivery valve configured to deliver hyperpolarized gas and at least one non-polarized gas to a subject;

monitoring a first pressure in the ventilator system upstream of the gas delivery valve;

monitoring a second pressure in the ventilator system downstream of the gas delivery valve;

obtaining a reading of the mass flow controller when the first pressure is substantially constant; and

automatically determining the tidal inspiration volume of hyperpolarized gas delivered to the subject *in situ* using the obtained mass flow controller reading.

28. A method according to Claim 27, wherein the ventilator system includes a variable flow rate mass flow controller disposed upstream of the gas delivery valve, said method further comprising automatically dynamically adjusting the flow rate of the mass flow controller to maintain a substantially constant first pressure during ventilation delivery of the hyperpolarized gas to the subject.

29. A method according to Claim 27, further comprising accepting user input to select a tidal volume operational mode with the desired tidal volume selected or a peak inspiration pressure operational mode with the desired peak inspiration pressure selected.

30. A method according to Claim 27, further comprising determining a fixed geometric volume based on pressure measurements taken while a distal end portion of the tracheal tube is closed, and subtracting the fixed geometric volume from the determined tidal volume.

31. A method according to Claim 27, further comprising selecting a desired ventilation delivery cycle with a breath per minute rate, a breath-hold duration and an inspiration/expiration ratio.

32. A method according to Claim 31, wherein the portion of the system upstream of the gas delivery valve has an associated fluid capacitance volume that is at least three times the volume of the lungs of the subject undergoing evaluation, said method further comprising controllably increasing and decreasing the fluid capacitance volume to stabilize the pressure upstream of the gas delivery valve to reduce the fluctuations in pressure between breaths.

33. A method according to Claim 32, further comprising triggering a MRI/NMR hyperpolarized gas signal acquisition sequence during a predetermined portion of the ventilation cycle when hyperpolarized gas is in the subject.

34. A method according to Claim 33, wherein the subject is a small animal.

35. A method according to Claim 34, wherein the selected breath per minute cycle is about 30 BPM during MRI/NMR signal acquisition.

36. A method according to Claim 34, further comprising obtaining a NMR/MRI signal having a signal strength and calibrating the NMR/NMR signal strength to the calculated tidal inspiration volume.

37. A method according to Claim 36, further comprising monitoring the temperature of the subject.

38. A method according to Claim 27, wherein the gas delivery valve is configured to selectively deliver hyperpolarized gas alone, non-polarized gas alone, and/or hyperpolarized gas combined with non-polarized gas, the method further comprising controlling the output of the first mass flow controller and a second mass flow controller to automatically provide desired blends of selected ventilation gases to the subject during non-polarized gas ventilation.

39. A method according to Claim 34, wherein the monitoring steps are carried out during an NMR spectroscopy and/or MRI imaging session.

40. A method according to Claim 27, wherein the hyperpolarized gas comprises hyperpolarized $^{129}Xe$.

41. A method according to Claim 27, wherein the hyperpolarized gas comprises hyperpolarized $^3He$.

42. A method according to Claim 27, wherein the gas delivery valve is configured to provide ventilation breath cycles of at least: (a) hyperpolarized Gas A inhale; (b) non-polarized Gas B inhale; (c) a combination of hyperpolarized Gas A and non-polarized Gas B inhale; (d) exhale; (e) partial exhale and hold; (f) hyperpolarized Gas A inhale and hold; (g) Gas B inhale and hold; and (h) a combination of hyperpolarized Gas A and Gas B inhale and hold.

43. A method according to Claim 42, wherein the gas delivery valve receives exhaust gas from the subject and vents the exhaust gas from the gas delivery valve.

44. A method according to Claim 27, wherein the tidal volume determination is carried out by subtracting a known fixed calibration volume from the total determined tidal volume.

45. A method according to Claim 44, wherein the tidal volume is calculated using the relationship expressed by equation (1):

flow rate / frequency = volume exhausted per cycle (1)

where "flow rate" is the flow rate of the mass flow controller when the first pressure is substantially constant and frequency is a selected breath per minute rate.

46. A method according to Claim 27, wherein the gas delivery valve comprises a plurality of gas actuation valves for actuating selectable gas output flow paths therein.

47. A method according to Claim 27, further comprising generating an estimated incremental decrease or increase of output flow rate that can provide a substantially constant first pressure based on the selected breath per minute rate and

an estimated delivered volume capacity associated with the type of animal undergoing analysis and adjusting the mass flow controller using the generated value.

48. A method according to Claim 27, further comprising generating a computer program library of *a priori* values of predicted animal volumetric characteristics and/or animal volumetric changes at a plurality of different peak inspiration pressures.

49. A method according to Claim 30, wherein the fixed geometric volume is determined for each size tracheal tubes used with the ventilator and/or for eacg species of subjects undergoing ventilation.

50. A system for delivering hyperpolarized gas to a subject, comprising:

a gas delivery valve configured to deliver hyperpolarized gas and at least one non-polarized gas to a subject;

a mass flow controller disposed upstream of the gas delivery valve;

a tracheal tube disposed downstream of the gas delivery valve;

means for monitoring a first pressure in the ventilator system upstream of the gas delivery valve;

means for monitoring a second pressure in the ventilator system downstream of the gas delivery valve;

means for automatically obtaining readings of the mass flow controller; and

means for automatically determining the tidal inspiration volume of hyperpolarized gas delivered to the subject *in situ* using the monitored first pressure and the value of a reading of the mass flow controller obtained when the first pressure is substantially constant.

51. A system according to Claim 50, wherein the ventilator system includes a variable flow rate mass flow controller disposed upstream of the gas delivery valve, said system further comprising means for automatically dynamically adjusting the flow rate of the mass flow controller to maintain a substantially constant

pressure at the first pressure sensor during delivery of the hyperpolarized gas to the subject.

52. A system according to Claim 50, further comprising:

means for accepting user input to select a tidal volume operational mode with the desired tidal volume selected or a peak inspiration pressure operational mode with the desired peak inspiration pressure selected; and

a second mass flow controller, wherein the first and second mass flow controllers are used to automatically provide desired blends of selected ventilation gases to the subject.

53. A computer program product for delivering hyperpolarized gas using a ventilator with an associated gas delivery valve and tracheal tube, the computer program product comprising:

computer program code that monitors a first pressure in the ventilator system upstream of the gas delivery valve;

computer program code that monitors a second pressure in the ventilator system downstream of the gas delivery valve;

computer program code that obtains a reading of a mass flow controller when the first pressure stabilizes at a substantially constant pressure; and

computer program code that calculates a tidal volume using the reading of the mass flow controller when the first pressure is substantially constant.

54. A computer program product according to Claim 53, wherein the ventilator system includes a variable flow rate mass flow controller disposed upstream of the gas delivery valve, and wherein said computer program product further comprises computer program code that automatically dynamically adjusts the flow rate of the mass flow controller to maintain a substantially constant first pressure during ventilation delivery of the hyperpolarized gas to the subject.

55. A computer program product according to Claim 54, further comprising computer program code for accepting user input to select from predetermined operational modes: (a) a tidal volume operational mode with the desired tidal volume selected; and (b) a peak inspiration pressure operational mode with the desired peak inspiration pressure selected.

56. A computer program product according to Claim 53, further comprising computer program code that selectively configures the gas delivery valve for inhale, exhale, or breath-hold operation.

57. A computer program product according to Claim 56, further comprising computer program code that selectively operates the gas delivery valve to output hyperpolarized gas alone, non-polarized gas alone, and/or a blend of hyperpolarized and non-polarized gas.

58. A computer program product according to Claim 53, further comprising computer program code that controllably actuates the gas delivery valve to select ventilation operation between at least: (a) hyperpolarized gas inhale; (b) non-polarized gas inhale; (c) a combination of hyperpolarized gas and non-polarized gas inhale; (d) exhale; (e) partial exhale and hold; (f) hyperpolarized gas inhale and hold; (g) non-polarized gas inhale and hold; and (h) a combination of hyperpolarized gas and non-polarized gas inhale and hold.

59. A computer program product according to Claim 57, wherein the hyperpolarized gas is a hyperpolarized noble gas, and wherein the non-polarized gas is a selected biocompatible non-polarized gas that inhibits depolarization of the hyperpolarized gas, and wherein the product further comprises computer program code that operates first and second mass flow controllers to automatically provide desired blends of selected ventilation gases to the subject.

60. A ventilator system having a ventilation flow path for ventilating a subject, comprising:

a gas delivery valve configured to selectively dispense a plurality of different gases to a subject;

a mass flow controller disposed upstream of the gas delivery valve;

a first polarized gas source in fluid communication with the gas delivery valve;

a second gas source in fluid communication with the gas delivery valve;

a first pressure sensor located upstream of the gas delivery valve;

a second pressure sensor located downstream of the gas delivery valve; and

a manifold line having a fluidic tunable capacitance disposed upstream of the gas delivery valve, wherein the fluidic capacitance has a volume that is at least about ten times greater than the volume of the lungs of the subject.

61. A ventilator system according to Claim 60, further comprising at least one fixed volume reservoir that is configured to selectively engage the manifold to adjust the fluidic capacitance responsive to pressure measurements obtained by the first and second pressure sensors.

62. A ventilator system according to Claim 60, further comprising a syringe with a quantity of fluid therein, the syringe being in communication with the manifold line and configured to selectively add or remove fluid from the manifold.

63. A ventilator system according to Claim 60, further comprising a second mass flow controller, wherein the first and second mass flow controllers are used to automatically provide desired blends of selected ventilation gases to the subject.